

REMARKS

Claims 1-6, 8-12, 15-17, and 19-22 are pending and were rejected in an office action mailed on June 3, 2004. Claims 1, 16, and 22 are amended as suggested by the Examiner, to correct typos and for clarity. No new matter has been added via amendment.

Reconsideration and allowance in view of the amendments and arguments respectfully are requested.

Definiteness Rejections

The Examiner has "maintained in part" a rejection for missing the word "immunization" after the word "genetic", for using the word "Target" before the word "polypeptide", and for clarity of step (c) in claim 1. The Examiner has suggested to amend claim 16 concurrently with claim 1. The Examiner also has rejected claim 22 for a confusion over "the solid phase matrix" v. "host cell." In response, applicants have amended claims 1 and 16 as suggested by the Examiner and amended claim 22 by deleting the phrase "incubated with" for clarity. Reconsideration and allowance respectfully are requested.

Obviousness Rejections

In view of the applicants' amendment to claim 1, the Examiner has withdrawn the obviousness rejections of claims 1-6, 8-12, and 15-17 made in view of Kilgannon *et al.* in combination with Content *et al.*, Letesson *et al.* and Whitehorn *et al.* Applicants thank the Examiner for the withdrawal.

However, on pages 5 to 7 of the office action, the Examiner has newly rejected claims 1-6, 8-12, 15-17, and 19-22 under new grounds and alleged as being unpatentable over Forster *et al.* in view of Content *et al.*, and further in view of Letesson *et al.* and Whitehorn *et al.*

In response, applicants respectfully traverse the rejection, which is insupportable as a matter of law and fact. In order to sustain a rejection for obviousness, the Examiner must show all of the recited claim elements in the combination of references that make up the rejection. When combining references to make out a *prima facie* case

of obviousness, the examiner is obliged to show by citation to specific evidence in the cited references that (i) there was a suggestion to make the combination and (ii) there was a reasonable expectation that the combination would succeed. Both the suggestion and reasonable expectation must be found within the prior art, and not be gleaned from applicants' disclosure. *In re Vaeck*, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991); *In re Dow Chemical Co.*, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988); see also MPEP §§ 2142-43 (Rev. 1, Feb. 2003). Applicants submit that the rejections do not meet this test.

In any event, a *prima facie* case of obviousness can be overcome by showing that (i) there are elements not contained in the references or within the general skill in the art, (ii) the combination is improper (for example, there is a teaching away or no reasonable expectation of success) and/or (iii) objective indicia of patentability exist (for example, unexpected results). See *U.S. v. Adams*, 383 U.S. 39, 51-52 (1966); *Gillette Co. v. S.C. Johnson & Son, Inc.*, 16 USPQ2d 1923, 1927 (Fed. Cir. 1990); *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve*, 230 USPQ 416, 419-20 (Fed. Cir. 1986).

Here, Forster *et al.* describe immunization of recombinant mammalian cells which have been transfected with a fusion protein bearing a myc tag. Forster *et al.* do not immunize directly with a DNA plasmid vector encoding a polypeptide of interest. Thus, the Forster disclosure alone, does not suggest the instant invention.

Although the Examiner has agreed that "Forster *et al.* does not teach the direct injection of DNA encoding the polypeptide ...", the Examiner nevertheless speculates that a skilled artisan would be able to arrive at the instant invention with a reasonable expectation of success by directly injecting into a mammal the expression vector encoding the fusion protein taught by Forster *et al.* Applicants respectfully disagree with the Examiner's speculation, which is based upon hindsight of knowing the instant invention. The instant invention is the first to combine the claimed methods, which includes putting an anchor (for example, GPI) into a vector that allows a transient cell surface attachment of the

polypeptide expressed *in vitro* to allow the transfected cells to be used as a solid phase to screen for the presence of antibodies.

The instant invention thus provides unique methods, which allow immunization or screening of antibodies against any polypeptide without having to isolate a recombinant polypeptide.

Regarding Content *et al.*, Letesson *et al.*, and Whitehorn *et al.*, applicants note that these secondary references describe "old elements" or the techniques that are well-known in the art. The Examiner presented no line of reasoning as to why the artisan reviewing the references would have found it obvious to selectively pick and choose various elements and/or concepts to arrive at the claimed invention. In making the rejection, the Examiner has done little more than cite references to show that one or more elements is known. The claimed invention, however, is clearly directed to a combination of elements. To support that the claimed combination is directed to obvious subject matter, either the references must expressly or impliedly suggest the claimed combination or the Examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in the light of teachings of the references. See *Ex parte Clapp*, 227 U.S.P.Q. 972 (B.P.A.I. 1985). Applicants also note that, casting an invention as "a combination of old elements", as the Examiner has done in making the rejections, leads improperly to an analysis of the claimed invention by the parts, not by the whole. See *Custom Accessories Inc., v. Jeffrey-Allan Industries, Inc.*, 807 F.2d 955, 1 U.S.P.Q.2d. 1196 (Fed. Cir. 1986).

Regarding Content *et al.*, applicants note that it discloses a DNA vaccine and a method of administering the DNA vaccine for prevention of tuberculosis (see Content *et al.* Abstract; col. 10-13). Content *et al.* do not disclose a method of producing antibodies or screening antibodies against a polypeptide without having to isolate a recombinant polypeptide. Also, Content *et al.* do not motivate one to combine the DNA vaccination with the recombinant mammalian cells producing a polypeptide of

interest.

Regarding Letesson *et al.*, applicants indicate that this reference discloses an *in vitro* method of detecting humoral immune response in *Brucella* infections, wherein recombinant proteins were purified with a polyhistidine tag and affinity chromatography for evaluation using an immunoassay (see Letesson *et al.* Abstract lines 5-7). The use of a "polyhistidine tag" in protein purification is a well-known technique; it is a so called "old element." Letesson *et al.* do not provide any motivation to apply the technique to modify any vector to express the polyhistidine tag. Letesson *et al.* uses microtiter plates and does not provide any direction or motivation to use any host cell surface to detect/purify the antibody binding to the fusion protein.

Whitehorn *et al.*, discloses a technique for expression and use of a tagged soluble version of cell surface receptors (see Whitehorn *et al.* page 1215). Thus, Whitehorn *et al.*, also teaches a well-known technique, another "old element." It does not, however, provide any direction or motivation to develop a process for antibody production or screening, as disclosed and claimed in the instant application.

Applicants further note that, Content *et al.*, Letesson *et al.*, or Whitehorn *et al.* fail to rectify the deficiencies in Forster *et al.* That is, the secondary references do not suggest or motivate one to combine them. Even if there was a motivation to combine these references, there would be no reasonable expectation of success in doing so. The Examiner's rejection is based upon hindsight, which is impermissible.

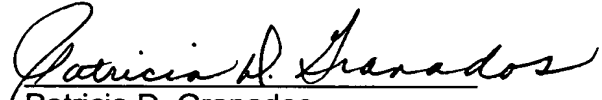
Therefore, the Examiner has failed to establish a *prima facie* case of obviousness. Withdrawal of the rejections is therefore, solicited.

CONCLUSION

In view of the instant amendments and remarks, reconsideration and allowance of all pending claims are requested. If there are any issues remaining that the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the local exchange listed below.

Respectfully submitted,

August 18, 2004
Date:


Patricia D. Granados
Reg. No.: 33,683

HELLER EHRMAN WHITE & McAULIFFE
1666 K Street, NW, Suite 300
Washington, DC 20006-1228
(202) 912-2142 (telephone)
(202) 912-2020 (facsimile)